Combined Effects of Spaceflight and Age in Astronauts as Assessed by Areal Bone Mineral Density and Trabecular Bone Score

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ABBREVIATIONS, ACRONYMS and TERMINOLOGY

- ARED Advanced Resistive Exercise Device (600 resistive pound force)
- DXA Dual-energy X-ray Absorptiometry
- IRED Interim Resistive Exercise Device (300 resistive pound force)
- Mir Russian Spacecraft
- MRI Magnetic Resonance Imaging
- QCT Quantitative Computed Tomography
- TVIS Treadmill Vibration Isolation System
- T2 Treadmill Exercise Hardware

INTRODUCTION

"Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: **bone density** and **bone quality**."

JAMA, 2001

"*…*an asymptomatic systemic bone disease characterized by low bone mass and **microarchitectural deterioration** of bone tissue, with a consequent increase in bone fragility and susceptibility of fracture"

Am J Med, 1993; Consensus Development Conference: diagnosis, prophylaxis, and treatment of osteoporosis

INTRODUCTION (Continued)

- The possibility for premature fragility fractures in astronauts – with prolonged exposure to space (>100 days) during their career – is a concern for the Bone Discipline at NASA Johnson Space Center
- To address this risk, the laboratory personnel of the Johnson Space Center's Bone & Mineral Laboratory monitors changes in skeletal health in astronauts with triennial measurements of areal bone mineral density by DXA
- This surveillance is performed during an astronaut's active years on spaceflight missions and during retirement years, or when the astronaut is no longer flying in space.
- In addition, pre and postflight DXA scans are performed for typical 6-month missions on the International Space Station
- Recently, astronauts on the International Space Station missions have been returning with postflight T-scores no less than -1.5 (for hip and spine)
- However, a precipitous loss in bone mineral density, over ~6 months, exceeds rates observed in comparable sites of the elderly over *1 year* (NASA Bone Summit, Orwoll et al., 2013).

INTRODUCTION (Continued)

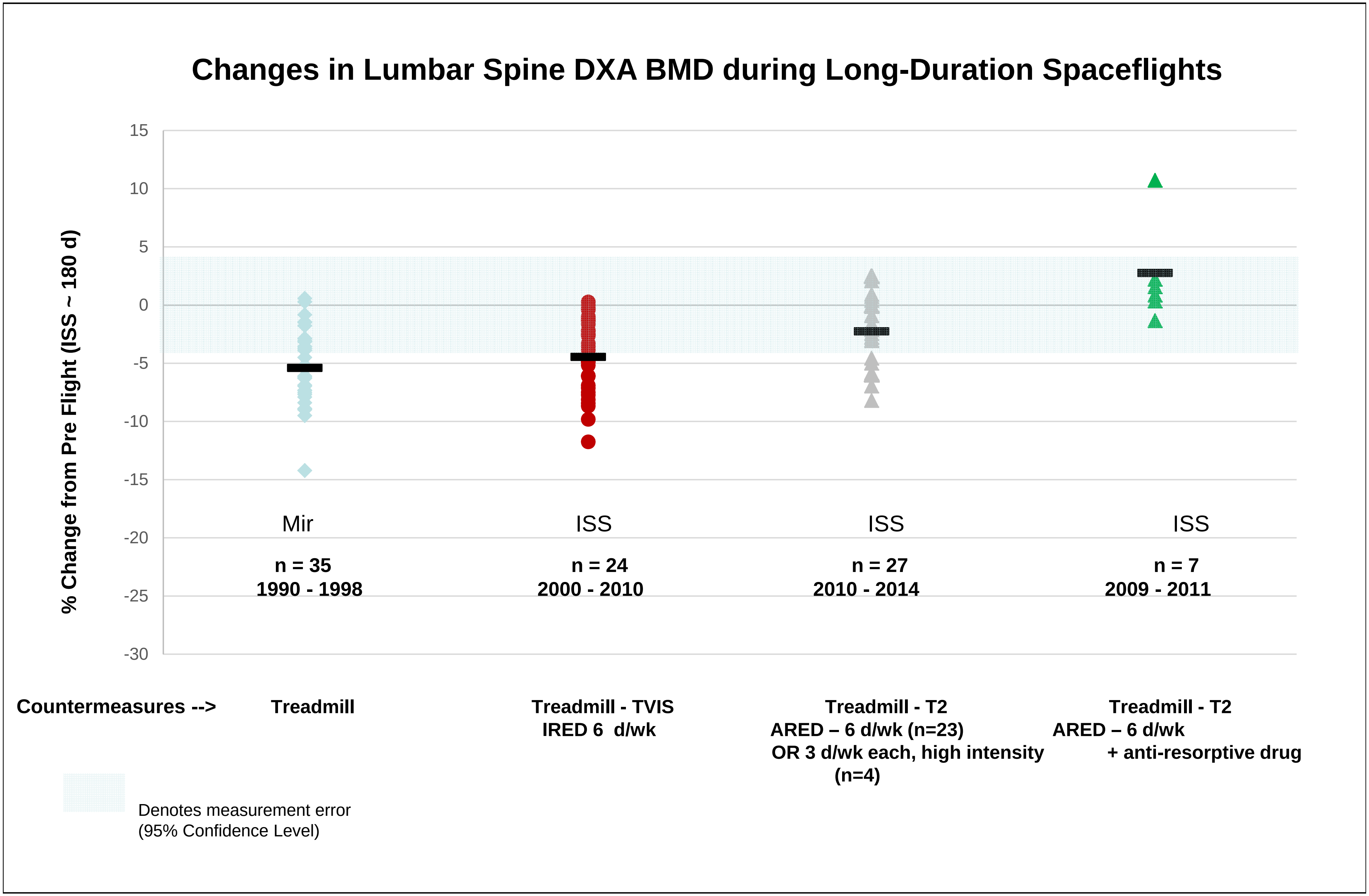
- This accelerated decline in bone mineral density suggests that there is a loss in connectivity in trabecular bone microarchitecture during spaceflight (NASA Bone Summit, Orwoll, 2013) that could predispose astronauts to vertebral compression fractures (Kleerekoper, 1985; Silva, 1997).
- We explored this risk by analyzing trabecular bone score in the archive of triennial DXA scans of astronauts.
- Trabecular bone score is derived from a method that measures grey-scale-level texture information extracted from lumbar spine DXA images. Its correlation with 3D parameters of bone microarchitecture suggests that it may be a useful for evaluating changes in connectivity.
- This novel index for bone microarchitecture of the spine may provide an index of bone quality that can further define the risk for fragility fractures in the astronaut as he/she ages.
- Previously, we reported that trabecular bone score detects an effect of ~6-month spaceflight independent of areal bone mineral density measurements (n=51 astronauts, 47+/-4 yr) (Smith et al., *J Clin Densitom*, 2014).
- In this report, we evaluated trends in the areal bone mineral density and in trabecular bone score to evaluate the combined effects of spaceflight and aging in retired astronauts

METHODS

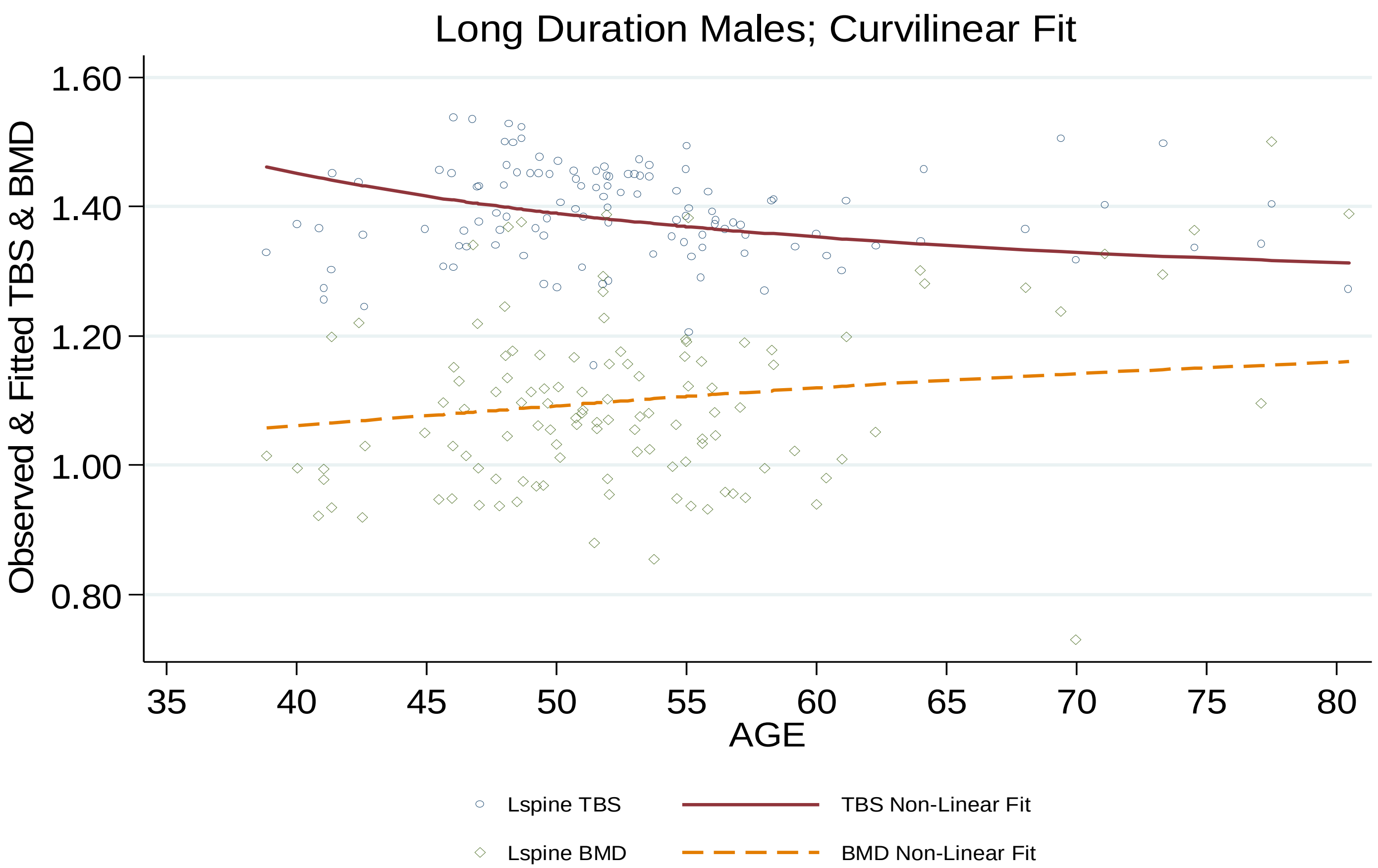
- Trends were evaluated in serial DXA scans of the lumbar spine (L1-4) obtained from a total of 311 individual astronauts (covered age range, 41 to 80 years; 302 males; 3 females)
- DXA scans were performed and analyzed on a Hologic Discovery W using the same technician for the pre and postflight scans
- Trabecular bone scores were generated by software) installed on the Johnson Space Center’s Hologic computer (MediMaps, Lausanne, Switzerland)
- Astronauts were categorized by the following spaceflight exposures:
  - Short-duration missions (<30 days)
  - Long-duration mission (>100 days)
  - Combined short- and long-duration missions

METHODS (Continued)

- Nonlinear models were applied to describe trends in *observations* (bone mineral density or trabecular bone score, not astronauts) plotted as a function of astronaut age
- We fitted 1175 observations of 311 astronauts, obtained from both pre- and postflight scans; observations denoted as “postflight” were from selected DXA scans obtained 3 years after landing or after astronaut’s bone mineral density was restored to within 2% of preflight, that is, a “recovered” state.
- Observations were then grouped and defined as follows:
  - Long duration: *after* exposure to *at least* 1 long-duration spaceflight >100 days
  - Short duration: *before* long duration and after exposure to at least 1 short-duration spaceflight <30 days
- Data trends for males and females were are reported separately

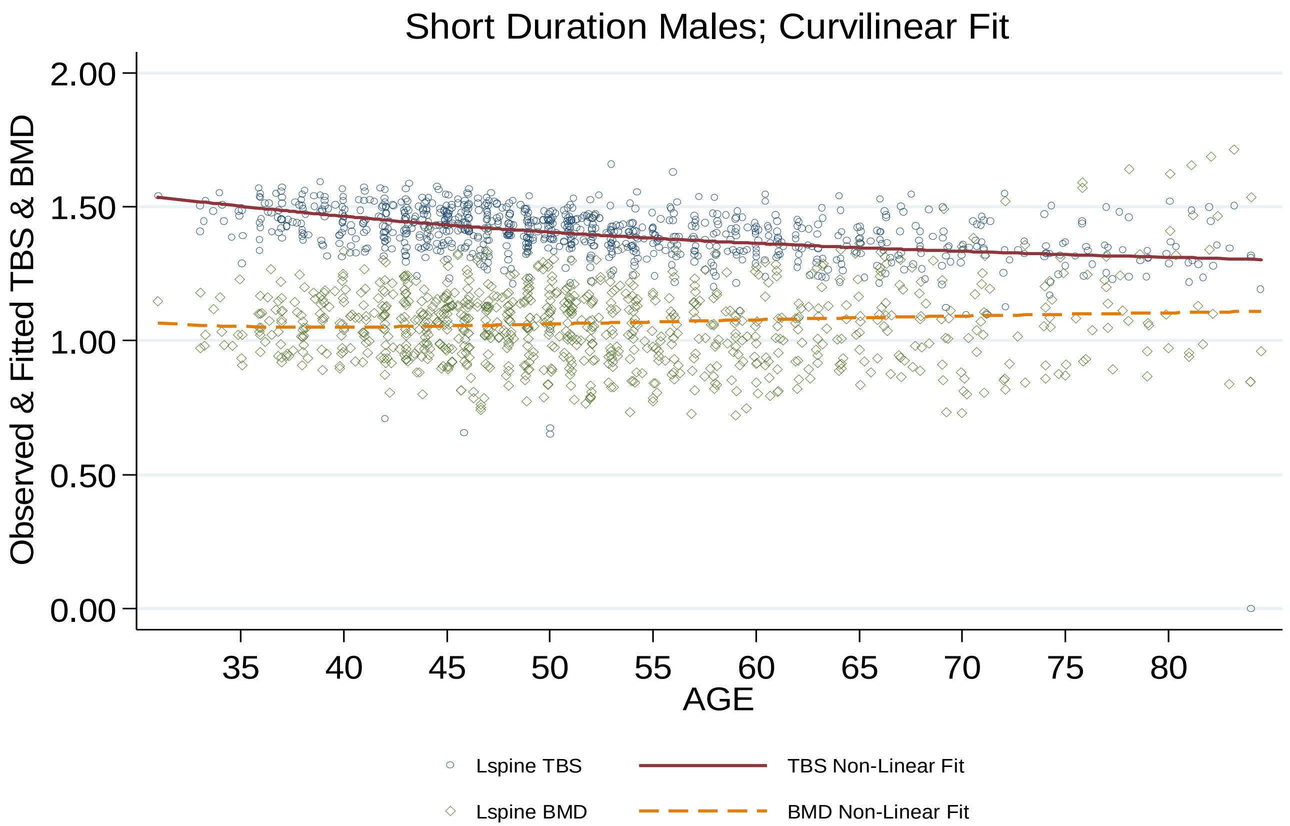

Changes in Lumbar Spine DXA BMD during Long-Duration Spaceflights
% Change from Pre Flight (ISS ~ 180 d)
15
10
5
0
-5
-10
-15
-20
-25
-30
Mir
n = 35
1990 - 1998
ISS
n = 24
2000 - 2010
ISS
n = 27
2010 - 2014
ISS
n = 7
2009 - 2011
Countermeasures -->
Treadmill
Treadmill - TVIS
IRED 6 d/wk
Treadmill - T2
ARED – 6 d/wk (n=23)
OR 3 d/wk each, high intensity
(n=4)
Treadmill - T2
ARED – 6 d/wk
+ anti-resorptive drug
Denotes measurement error
(95% Confidence Level)

RESULTS (Placeholder)



Only observations following at least one long-duration spaceflight, and after established BMD recovery (within 2% of baseline or 3 years post-flight) were used for fitting, and are graphed here

(Insert Data figure)



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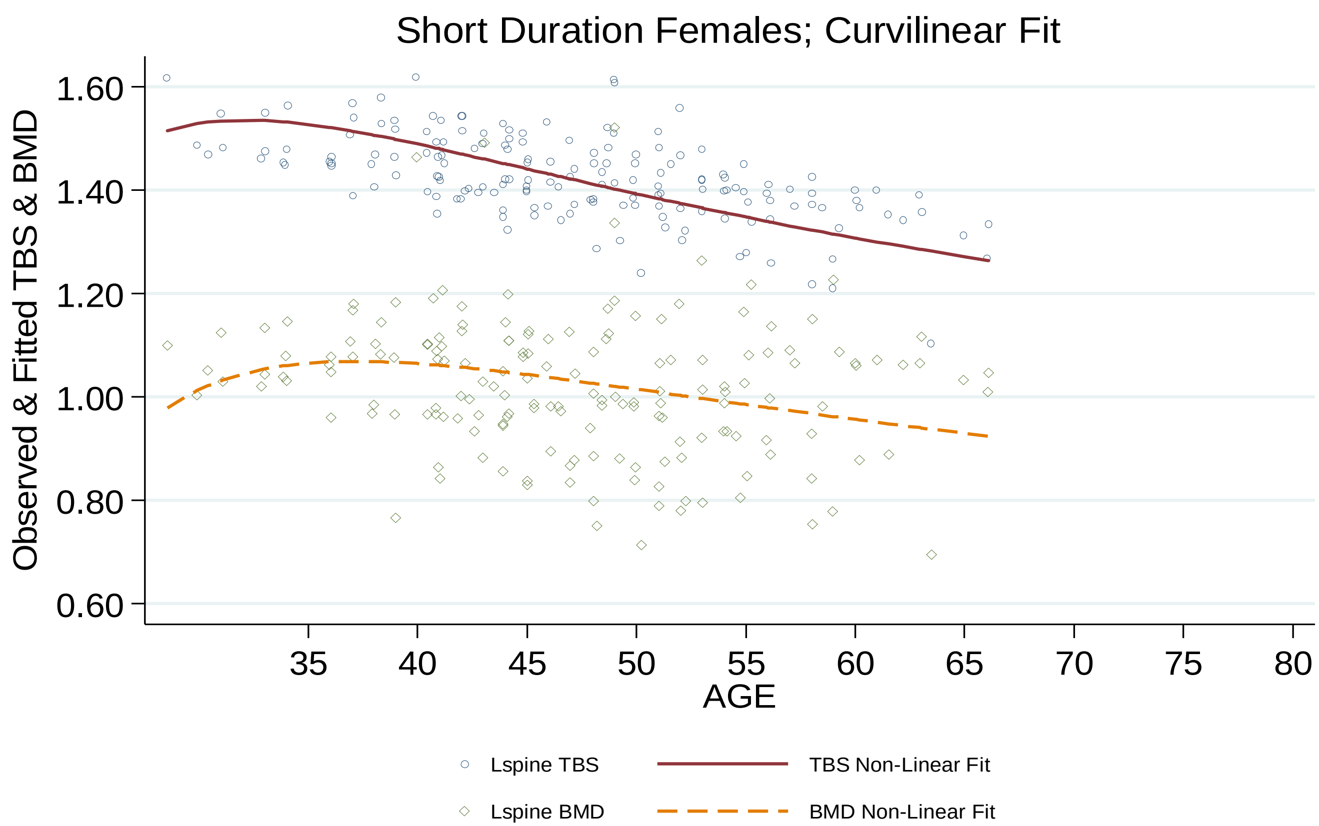
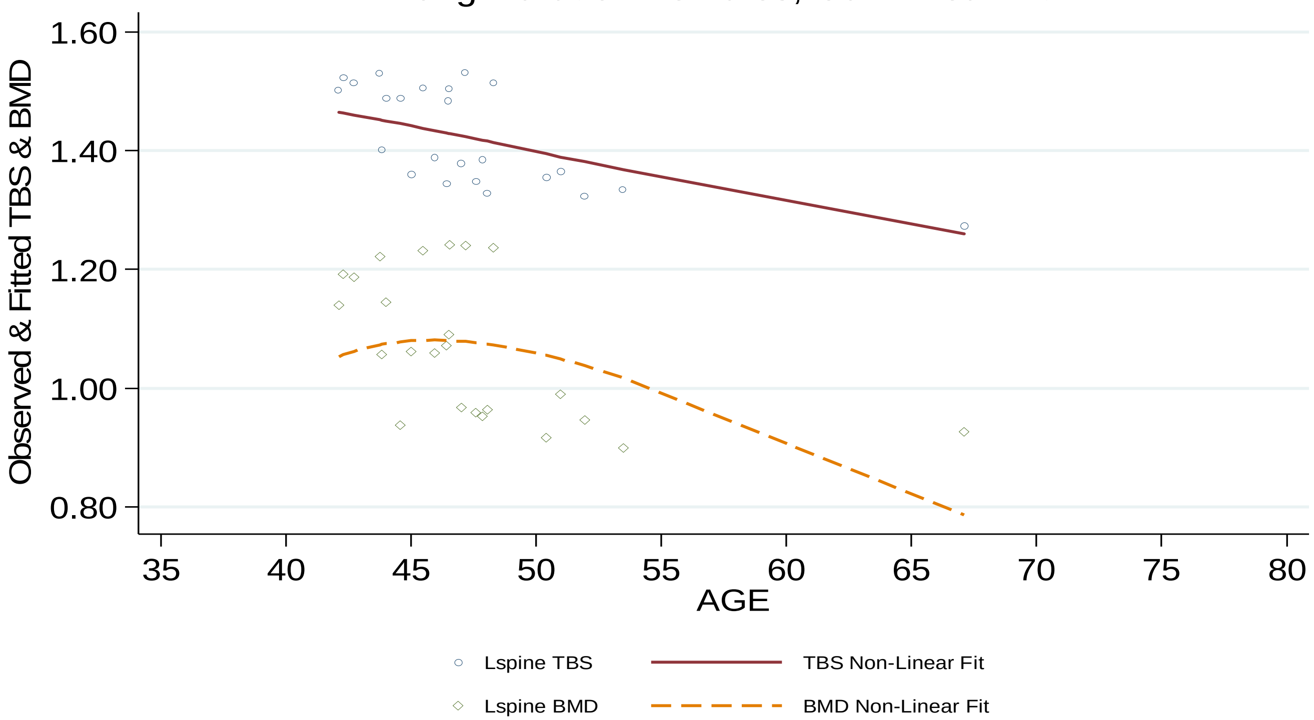


There aren't a lot of data at ages>55, and the model suffers for that.

Long Duration Females; Curvilinear Fit



There aren't a lot of data at ages>55, and the model suffers for that.

DISCUSSION

Our models of:

- Short-duration observations revealed that trabecular bone score and bone mineral density had similar curvilinear declines with age for both male and female astronauts
- Long-duration observations showed trabecular bone score declining with age while bone mineral density appeared stable or trending upward
- Female (n=8) long-duration observations were too few to discern a trend

Trabeculae cannot be replaced or reconnected if lost or completely separated (Parfitt et al., 1987); disconnected trabeculae is an underlying cause of vertebral compression fractures (Kleerekoper, 1985; Parfitt, 1987) and of reduced vertebral bone strength (Silva, 1997). Hence, a capability to monitor changes in trabecular bone microarchitecture of the spine is required for possible intervention, that is, before irreversible changes have occurred.

DISCUSSION (Continue)

- Trabecular bone score enables an analysis of active astronauts with minimal impact on launch schedules and facilitates a retrospective analysis of archived DXA scans. Multiple studies validating the clinical utility of trabecular bone score are emerging in terrestrial clinical research to inform the trabecular bone score interpretation. This study suggests that trabecular bone score captures the combined effects of age and of spaceflight on bone microarchitecture independent from changes in areal bone mineral density.
- Limitations:
  - Evaluated trends in data observations and not in individual astronauts
  - Astronauts population and fracture incidence are low and not likely to reach the required level of evidence to identify an intervention threshold
  - Baseline bone mineral density of trabecular compartment of the lumbar spine of astronauts may be too high to detect micro-architectural degradation
  - The data from females were too scarce (<10) to discern the combined effect of menopause and spaceflight

CONCLUSION

Trabecular bone score may provide an additional index for the lumbar spine to monitor the combined changes due to spaceflight and due to aging on bone quality. This increased knowledge may enhance the ability to identify an intervention trigger for premature vertebral fractures in astronauts in addition to areal bone mineral density.

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BACKUP

The following reported studies support a study of trabecular bone score as an index for bone microarchitecture in DXA scans of astronauts.

1. Comparison to gold-standard method:
   - Guggenbuhl P et al., *Osteoporos Int*. 2006;17(3):447-54.
   - Hans D et al., *J Clin Densitom*. 2011 Jul-Sep;14(3):302-12.
2. Tested in case-control studies:
   - Winzenrieth R et al., *Calcif Tissue Int*. 2010 Feb;86(2):104-9
   - Lespessailles E, et al., *Osteoporos Int*. 2008 Jul;19(7):1019-28
   - Del Rio LM et al., *Osteoporos Int*. 2013 Mar;24(3):991-8. doi: 10.1007/s00198-012-2008-8.
3. Evaluated in prospective studies with fracture outcome:
   - Bréban S et al., *J Clin Densitom*. 2012 Jul-Sep;15(3):260-6
   - Hans D et al., *J Bone Miner Res*. 2011 Nov;26(11):2762-9